REMARKS

After entry of this amendment, claims 1, 5, 6, 18-21, and 28-34 are pending. New claim 28 has been added and finds support in the specification, for example, at page 33, Example 2. New claims 29-34 have been added and find support *inter alia* in the original claims. The claims have been amended without prejudice or disclaimer and find support *inter alia* in the original claims. No new matter has been added.

Claim Rejection – 35 U.S.C. § 112, First Paragraph

The Examiner reinstates the nonenablement rejection to claims 1, 5, 6, and 18-21.

The Examiner contends that, although the specification discloses that the deposit has been made, it is unclear from the record whether a statement indicating that the deposit was accepted under the terms of the Budapest Treaty and that the deposited material will be irrevocably and without restriction or conditions released to the public upon issuance of the patent. Applicants respectfully disagree and traverse the rejection.

However, to expedite prosecution, Applicants enclose herewith the receipts of deposit issued by the depository. As shown by the enclosed receipts of deposit, samples of microorganisms were deposited under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure with the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ), Inhoffenstraÿe 7 B, 38124 Braunschweig, Germany. The deposit of microorganisms was made on July 11, 2003, accepted by the DSMZ, tested by the DSMZ, and shown to be viable, and assigned DSMZ accession numbers DSM 15751, 15752, 15753, 15754, and 15755.

In accordance with MPEP § 2410.01 and 37 CFR § 1.808, assurance is hereby given that all restrictions on the availability to the public of the microorganisms at DSMZ accession numbers DSM 15751, 15752, 15753, 15754, and 15755 will be irrevocably removed upon the grant of a patent based on the instant application, except as permitted under 37 CFR § 1.808(b). The deposits were viable at the time of deposit. The deposits will be replaced if they should ever become non-viable. During pendency of this application, access to the deposits will be afforded to the Commissioner upon request. The enclosed deposit receipts attest to the fulfillment of the criteria set forth in 37 CFR §§ 1.801 – 1.809.

In view of the enclosed receipts of deposit and the above certification, it is believed that this rejection is overcome. Reconsideration and withdrawal of the rejection is respectfully requested.

Claim Rejection – 35 U. S.C. § 112, Second Paragraph

Claims 1, 5, 6, and 18-21 are rejected as being indefinite.

The Examiner alleges that claim 1 is confusing because the preamble recites isomerization of numerous compounds while the body of the claim directs to an isomerization by *Lactobacillus or Lactococcus* that is capable of racemizing at least one compound selected from only five compounds. The Examiner thus concludes that the correlation between the recited capabilities of the microorganisms and the compounds intended to be bioconverted as recited in the preamble cannot be ascertained. Applicants respectfully disagree.

It is noted initially that the five compounds recited in the body of the claim are intended to define the specific racemization function of the microorganisms suitable for the claimed method while the compounds recited in the preamble of the claim are to further define the claimed method. It is further noted that the term "capable of" does not necessarily mean "only able to." Accordingly, it is respectfully submitted that the claim is unambiguously clear to one skilled in the art as being drawn to a method for the microbiological isomerisation of the compounds of formula I. Such isomerisation is catalyzed by the enzymatic activity contained in either intact cells or extracts of microorganisms of the genus *Lactobacillus*. The recitation of "capable of racemizing at least one compound selected from . . ." at the end of claim 1 is to further define the microorganisms of the genus *Lactobacillus* that are suitable for use in the claimed method. This is further confirmed by Example 2 at pages 33-34 of the specification which essentially describes a screening method by which microorganisms containing the suitable racemase activity are obtained.

In view of the above remarks, reconsideration and withdrawal of the rejection is respectfully requested.

The Examiner rejects claim 6 as being confusing for reciting different DSM accession number in parenthesis. In response, claim 6 has been amended without prejudice or disclaimer to recite the microorganisms with more specification. In view of the present amendment, it is

believed that this rejection is overcome. Reconsideration and withdrawal of the rejection is respectfully requested.

Claim Rejections – 35 U.S.C. §103(a)

Claims 1, 5, 6, and 18-21 remain rejected over Stetter *et al.* (hereinafter "Stetter"), in view of DSMZ catalogue, Mori *et al.* (hereinafter "Mori") and Seufer-Wasserthal *et al.* (hereinafter "Seufer-Wasserthal").

The Examiner relies on Stetter for teaching a process of isomerization of an alpha-hydroxycarboxylic acid with *Lactobacillus* strains, especially *Lactobacillus* strains that correspond to DSM 15753, 15754, and 15755 used in the present application, as demonstrated by DSMZ catalogue. The Examiner identifies the difference between the process taught in Stetter and the claimed process as being the substrates submitted to the isomerization reaction. However, the Examiner asserts that one skilled in the art would recognize that the substrate specificity of the enzyme extracts or microbial cells provided by Stetter is not limited to the disclosed subtract and would have been motivated to test more substrates with a reasonable expectation of success. To support such a position, the Examiner relies on Mori for suggesting further substrates such as D-mandelic acid as being useful raw materials or intermediates in the preparation of pharmaceuticals.

The Examiner further acknowledges that the teaching of Stetter differs from the claimed subject matter in that further enzymatic or chemical modifications are not recited. The Examiner, however, relies on Mori for showing that it was known in the art to modify compounds obtained in isomerization or resolution reactions by converting a racemic compound into an optically active isomer. Additionally, the Examiner also relies on Seufer-Wasserthal for disclosing the chemical or enzymatic enantioselective subsequent reaction that comprises esterification.

The Examiner thus concludes that it would have been obvious to one skilled in the art to modify the process taught in Stetter by using a variety of *Lactobacillus* strains and substrates such as mandelic acid as suggested by Mori and subjecting the resultant product to further modification reactions as suggested by Mori and Seufer-Wasserthal. The Examiner contends that a skilled artisan would have been motivated to do so for the expected benefit of obtaining

pharmaceutically valuable optically active compounds or useful intermediates for producing such compounds. Applicants respectfully disagree and traverse the rejection.

It is noted initially that not every *Lactobacillus* strain possesses a positive racemization activity as required by the claims. As illustrated in Example 2 and Table 6 at pages 33-34 of the specification, among the *Lactobacillus* strains tested, only a few showed a positive racemization activity with the substrates used in the exemplified screening procedure. Moreover, it is rather a surprising discovery of the present application that the *Lactobacillus* strains suitable for the claimed method possesses a positive racemization activity for a panel of structurally different substrates such as hydroxyisocaproic acid, 2-hydroxy-3-methylbutanoic acid and 2-hydroxy-4-phenylbutyric acid. Applicants are not aware of any prior art reference teaching or suggesting a suitable procedure for screening and obtaining the *Lactobacillus* strains with such racemization activity. Accordingly, it is respectfully submitted that, contrary to the Examiner's assertion, a skilled artisan would not have a reasonable expectation of success to arrive at the claimed subject matter by simply using a variety of *Lactobacillus* strains in the process taught in Stetter.

Furthermore, as illustrated by the enclosed references, all of which concern lactate racemase, the scientific community in the field of the claimed subject matter was actually not aware of the surprising extended racemization activity of certain microorganisms, in particular microorganisms of the genus *Lactobacillus*, prior to the filing date of the present application.[1] For instance, Schnell *et al.* stated in their review article that was published immediately prior to the priority date of the present application, that "the substrate tolerance of lactate racemase is unknown." See Schnell *et al.*, at page 656, right Col., last paragraph. While providing an extensive discussion regarding mandelate racemase and its different substrates, Schnell *et al.* were obviously reluctant to make any prediction or suggestion with respect to any potential or possible extended subtract spectrum for lactate racemase.

Without knowing such extended racemization activity, one of ordinary skill in the art would not have been motivated to use the microorganisms with such specific racemization

[1] For the Examiner's convenience, a Listing of References summarizing the literature relating to lactate racemase that is relied on by Applicants is attached with this response. The information provided in the Listing includes the name of the first author, the publication year, relevant passages of the disclosure, the substrate used, as well as the microbial source investigated. If necessary, Applicants can re-submit these references in form of an Information Disclosure Statement.

activity to isomerize structurally different analogues of lactic acid as being done by the inventors of the present application. With this regard, Applicants note that it is well established that "obviousness cannot be predicated on what is unknown." *In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993). As found by the court in *In re Antonie*, which reversed the Board's finding of obviousness, it is the invention as a whole, and not some part of it, which must be obvious under 35 U.S.C. § 103. *In re Antonie*, 559 F.2d 618, 619-620 (CCPA 1977); see also MPEP § 2141.02 V. Furthermore, the court in *In re Antonie* found that the prior art did not reveal the property which appellant discovered and, therefore, there was no basis to find obviousness. *Id.* See also *In re Naylor*, 369 F.2d 765, 768 (CCPA 1966) (reversing the Board's finding of obviousness and holding that one skilled in the art ***must have recognized*** the claimed property would have been the inevitable result of obvious modification.).

Because the surprising property was not known in the art at the time the invention was made, and because one of ordinary skill in the art would not have been motivated to use a variety of *Lactobacillus* strains in the process taught in Stetter with a reasonable expectation of success to arrive at the claimed subject matter, it is respectfully submitted that the cited references, alone or in combination, do not render the claims as amended obvious. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Separate consideration to new claims 28-34 is respectfully requested. Applicants submit that none of the cited references teaches or suggests the screening step recited in new claim 28. As such, a *prima facie* case of obviousness is not established.[2]

CONCLUSION

In view of the above remarks and further in view of the above amendments, Applicants respectfully request withdrawal of the rejections and allowance of the claims. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number given below.

Applicants reserve all rights to pursue the non-elected claims and subject matter in one or more divisional applications, if necessary.

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[2] To support a *prima facie* conclusion of obviousness, the prior art must disclose or suggest all the limitations of the claimed invention. See *In re Lowry*, 32 F.3d 1579, 1582, 32 USPQ2d 1031, 1034 (Fed. Cir. 1994); see also *Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341 (Fed. Cir. 2008) ("[t]he KSR opinion . . . did not mention or affect the

Accompanying this response is a petition for a one-month extension of time to and including December 14, 2009 pursuant to 37 CFR § 1.7(a) with the required fee authorization. No further fees are believed due. However, if any additional fee is due, the Director is hereby authorized to charge our Deposit Account No. 03-2775, under Order No. 13111-00027 US from which the undersigned is authorized to draw.

Respectfully submitted,

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Attachments:

1. Receipts of deposit for DSMZ accession numbers DSM 15751, 15752, 15753, 15754, and 15755.
2. Listing of References summarizing the literature relating to lactate racemase relied on by Applicants in the present response and copies of the references. If necessary, Applicants can re-submit these references in form of an Information Disclosure Statement.

requirement that ***each and every claim limitation be found present in the combination of the prior art references before the analysis proceeds***.") (emphasis added).